

Identification, organization and characterization of ZNF genes in a 4 MB cluster on 19p12.

Harvey W. Mohrenweiser¹, Susan M. G. Hoffman², Dominique Poncelet³, Joseph Martial³ and Evan E. Eichler¹.

¹ Human Genome Center, Lawrence Livermore National Labs, Livermore, CA, ² Miami Ohio University, Miami, OH, ³ Laboratoire de Biologie Moleculaire et de Genie Genetique, Universite de Liege, Belgium.

Zinc finger (ZNF) genes represent one of the largest and most diverse gene family in the human genome, constituting approximately 0.01% of human genetic material. Chromosome 19 appears to be particularly enriched for zinc finger genes, such that one third of all ZNF loci are distributed within three clusters corresponding to cytogenetic band locations 19p12, p13.2 and q13.4. We are currently mapping and characterizing all ZNF genes in the 4 MB 19p12 cluster, located between STS markers D19S269 and D19S450. Long-range inter-Alu PCR of a contig of overlapping 19p12 YAC clones has been used to identify 300 cosmids and 15 BAC's which map to this region. Nineteen cosmid contigs have been constructed comprising approximately 2.9 MB of this 4 MB interval. The location of cosmid contigs was confirmed using FISH and cosmids were anchored using an STS marker screening strategy. To define the architecture of the 19p12 ZNF cluster, probes corresponding to various ZNF91 exons were used to screen Southern blots of EcoRI-digested genomic clones. This analysis identified a minimum of 30 potential KRAB (Kruppel-related associated box) ZNF genes in this region. The genes appear to be arranged in head-to-tail organization, with duplcon sizes ranging from 100 to 180 kb. Near the promoter of virtually all 19p12 ZNF genes, human endogeneous retrovirus (HERV) elements have been identified, suggesting that these elements were tandemly duplicated along with the ZNF cluster. Comparative sequencing and retroposon-mapping indicate that these duplications occurred approximately 35-50 mya. Hybridization and sequence analysis has confirmed the identity, thus far, of five functional zinc finger genes.

***Performed under auspices of the US DOE by LLNL; contract No. W-7405-ENG-48.**